UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, DC 20460

OFFICE OF CHEMICAL SAFETY
AND POLLUTION PREVENTION

December 23, 2011

MEMORANDUM

Subject: Efficacy Review for EPA Reg. No. 777-117, Edelweiss Trigger;
DP Barcode: 395793

From: Tajah Blackburn, Ph.D., Microbiologist
Efficacy Evaluation Team
Product Science Branch
Antimicrobials Division (7510P)

12/23/11

To: Marshall Swindell PM33/Martha Terry
Regulatory Management Branch I
Antimicrobials Division (7510P)

Applicant: Reckitt Benckiser
Morris Corporate Center IV
399 Interpace Parkway
Parsippany, NJ 07054-0225

Formulation from the Label:

Active Ingredient(s)	% by wt.
Hydrogen Peroxide	0.88%
Other Ingredients	99.12%
Total	100.00%

I BACKGROUND

The product, Edelweiss - Trigger (EPA Reg. No. 777-117), is an EPA-approved disinfectant (bactericide, fungicide, virucide) and deodorizer for use on hard, non-porous surfaces in household, commercial, institutional, industrial, food preparation, and hospital or medical environments. The data package included efficacy data demonstrating product effectiveness as a disinfectant against *Staphylococcus aureus*, *Salmonella enterica*, *Pseudomonas aeruginosa*, Rhinovirus type 37, and Rotavirus. Studies were conducted at ATS Labs, located at 1285 Corporate Center Drive, Suite 110, in Eagan, MN 55121.

This data package contained a letter from the applicant to EPA (dated May 4, 2011), EPA Form 8570-35 (Data Matrix), four studies (MRID 486034-02 through 486034-05), Statements of No Data Confidentiality Claims for all four studies, and the proposed label.

II USE DIRECTIONS

The product is designed for disinfecting hard, non-porous surfaces, including: appliance exteriors, bathtubs, bed frames, cabinets, chairs, changing tables, computer screens, counters, cribs, diaper pails, doorknobs, drawers, exhaust fans, faucet, fixtures, floors, garbage cans, grill exteriors, high chairs, laundry hampers, light fixtures, metal blinds, mirrors, outdoor patio furniture, patio doors, piano keys, picnic tables, shelves, shower curtains, shower doors, shower stalls, sinks, tables, telephones, television screens, toilet bowls, urinals, vanity tops, wall paper, walls, water fountains, and windows. The proposed label indicates that the product may be used on hard, non-porous surfaces, including: Corian, crystal, enamel, Formica, fiberglass (fixtures), glass, glazed ceramic, glazed porcelain, glazed tile, laminate, linoleum, metal (i.e., aluminum, chrome, copper, stainless steel, tin), painted woodwork, plastic laminate, sealed granite, sealed marble, and vinyl. Directions on the proposed label provide the following information regarding use of the product as a disinfectant: Pre-clean surface. Spray surface until thoroughly wet. Leave for 10 minutes before wiping.

III AGENCY STANDARDS FOR PROPOSED CLAIMS

<u>Disinfectants for Use on Hard Surfaces in Hospital or Medical Environments</u>

The effectiveness of disinfectants for use on hard surfaces in hospital or medical environments must be substantiated by data derived using the AOAC Use-Dilution Method (for water soluble powders and liquid products) or the AOAC Germicidal Spray Products as Disinfectants Method (for spray products). Sixty carriers must be tested with each of 3 product samples, representing 3 different product lots, one of which is at least 60 days old, against *Salmonella enterica* (ATCC 10708; formerly *Salmonella choleraesuis*), *Staphylococcus aureus* (ATCC 6538), and *Pseudomonas aeruginosa* (ATCC 15442). To support products labeled as "disinfectants," killing on 59 out of 60 carriers is required to provide effectiveness at the 95% confidence level.

Virucides

The effectiveness of virucides against specific viruses must be supported by efficacy data that simulates, to the extent possible in the laboratory, the conditions under which the product is intended to be used. Carrier methods that are modifications of either the AOAC Use-Dilution Method (for liquid disinfectants) or the AOAC Germicidal Spray Products as Disinfectants Method (for spray disinfectants) must be used. To simulate in-use conditions, the specific virus to be treated must be inoculated onto hard surfaces, allowed to dry, and then treated with the product according to the directions for use on the product label. One surface for each of 2 different product lots of disinfectant must be tested against a recoverable virus titer of at least 10^6 from the test surface for a specified exposure period at room temperature. Then, the virus must be assayed by an appropriate virological technique, using a minimum of four determinations per each dilution assayed. Separate studies are required for each virus. The calculated viral titers must be reported with the test results. For the data to be considered acceptable, results must demonstrate complete inactivation of the virus at all dilutions. When cytotoxicity is evident, at least a 3-log reduction in titer must be demonstrated beyond the cytotoxic level.

IV COMMENTS ON THE SUBMITTED EFFICACY STUDIES

1. MRID 486034-02 "AOAC Germicidal Spray Method," Test Organisms: *Staphylococcus aureus* (ATCC 6538) and *Salmonella enterica* (ATCC 10708), for Edelweiss Trigger Formula 1563-125A, by Nicole Albert. Study conducted at ATS Labs. Study completion date – September 8, 2011. Study Identification Number A11707.

This study was conducted against *Staphylococcus aureus* (ATCC 6538) and *Salmonella enterica* (ATCC 10708). Three lots (Lot Nos. 1754-080, 1754-081, and 1754-082) of the product, Edelweiss Trigger Formula 1563-125A, were tested using the AOAC Germicidal Spray Products as Disinfectants Method as described in the AOAC Official Methods of Analysis, 2009. At least one of the product lots tested (i.e., Lot No. 1754-082) was at least 60 days old at the time of testing. Testing was performed on July 18, 2011 and August 31, 2011. The product was received ready-to-use, as a trigger spray. Cultures of the challenge microorganisms were prepared in accordance with the published AOAC method. The product was not tested in the presence of a 5% organic soil load. Sixty (60) glass slide carriers (18 mm x 36 mm) per product lot per microorganism were inoculated with 10.0 µL of a 48-54 hour old suspension of test organism. Inoculum was uniformly spread over the entire surface of each carrier. The carriers for *Staphylococcus aureus* were dried for 40 minutes at 35-37°C at 50% relative humidity. The carriers for *Salmonella enterica* were dried for 30 minutes at 35-37°C at 50% relative humidity. For each lot of product, separate carriers were sprayed (3 sprays) with the product from a distance of 6-8 inches from the carrier surface. The carriers were allowed to remain wet for 10 minutes at 21-22°C at 65-68% relative humidity. Following the exposure period, the remaining liquid was drained from each carrier. Individual carriers were transferred to 20 mL of Letheen Broth with 0.1% sodium thiosulfate and 0.01% Catalase to neutralize. [It is unknown whether tubes containing neutralizer were shaken thoroughly after addition of the carriers, as specified in the AOAC method.] All subcultures were incubated for 48±2 hours at 35-37°C. Subcultures from testing on August 31, 2011 were examined for visible growth after ~1 day of incubation, and then re-incubated for ~1 day for a total of 48±2 hours of incubation.

Following incubation, the subcultures were examined for the presence or absence of visible growth. Controls included those for carrier population, purity, sterility, viability, and neutralization confirmation (all three product lots).

2. MRID 486034-03 "AOAC Germicidal Spray Method," Test Organism: *Pseudomonas aeruginosa* (ATCC 15442), for Edelweiss Trigger Formula 1563-125A, by Nicole Albert. Study conducted at ATS Labs. Study completion date – September 8, 2011. Study Identification Number A11708.

This study was conducted against *Pseudomonas aeruginosa* (ATCC 15442). Three lots (Lot Nos. 1754-080, 1754-081, and 1754-082) of the product, Edelweiss Trigger Formula 1563-125A, were tested using the AOAC Germicidal Spray Products as Disinfectants Method as described in the AOAC Official Methods of Analysis, 2009. At least one of the product lots tested (i.e., Lot No. 1754-082) was at least 60 days old at the time of testing. Testing was performed on July 18, 2011 and August 31, 2011. The product was received ready-to-use, as a trigger spray. A culture of the challenge microorganism was prepared in accordance with the published AOAC method. The product was not tested in the presence of a 5% organic soil load. Sixty (60) glass slide carriers (18 mm x 36 mm) per product lot were inoculated with 10.0 µL of a 48-54 hour old suspension of test organism. Inoculum was uniformly spread over the entire surface of each carrier. The carriers were dried for 38-40 minutes at 35-37°C at 50% relative humidity. For each lot of product, separate carriers were sprayed (3 sprays) with the product from a distance of 6-8 inches from the carrier surface. The carriers were allowed to remain wet for 10 minutes at 21-22°C at 64-68% relative humidity. Following the exposure period, the remaining liquid was drained from each carrier. Individual carriers were transferred to 20 mL of Letheen Broth with 0.1% sodium thiosulfate and 0.01% Catalase to neutralize. [It is unknown whether tubes containing neutralizer were shaken thoroughly after addition of the carriers, as specified in the AOAC method.] All subcultures were incubated for 48±2 hours at 35-37°C. Subcultures from testing on August 31, 2011 were examined for visible growth after ~1 day of incubation, and then re-incubated for ~1 day for a total of 48±2 hours of incubation. Following incubation, the subcultures were examined for the presence or absence of visible growth. Controls included those for carrier population, purity, sterility, viability, and neutralization confirmation (all three product lots).

Note: Protocol deviations/amendments reported in the study were reviewed.

3. MRID 486034-04 "Virucidal Efficacy of a Disinfectant for Use on Inanimate Environmental Surfaces, Virus: Rhinovirus type 37" for Edelweiss Trigger Formula 1563-125A, by Mary J. Miller. Study conducted at ATS Labs. Study completion date – September 6, 2011. Study Identification Number A11718.

This study was conducted against Rhinovirus type 37 (Strain 151-1; ATCC VR-1147), using MRC-5 cells (human embryonic lung fibroblasts; ATCC CCL-171; propagated in-house) as the host system. Two lots (Lot Nos. 1754-080 and 1754-081) of the product, Edelweiss Trigger Formula 1563-125A, were tested according to ATS Labs Protocol No. SRC53070811.R37.2 (copy provided). The product was received

ready-to-use, as a trigger spray. The stock virus culture was adjusted to contain 1% fetal bovine serum as the organic soil load. Films of virus were prepared by spreading 0.2 mL of virus inoculum uniformly over the bottoms of separate sterile glass Petri dishes. The virus films were air-dried for 20 minutes at 15.5°C at 50% relative humidity. For each lot of product, separate dried virus films were sprayed (3 pumps) with the product from a distance of 6-8 inches from the carrier surface until thoroughly wet. The carriers were allowed to remain wet for 10 minutes at 21.0°C. Just prior to the end of the exposure time (≤15 seconds), the plates were scraped with a cell scraper to re-suspend the contents. The virus-disinfectant mixtures were passed immediately through individual Sephadex columns, and diluted serially in Minimum Essential Medium with 10% (v/v) heat-inactivated fetal bovine serum, 10 µg/mL gentamicin, 100 units/mL penicillin, and 2.5 µg/mL amphotericin B. MRC-5 cells in multi-well culture dishes were inoculated in quadruplicate with 0.1 mL of the dilutions. The cultures were incubated at 31-35°C in a humidified atmosphere of 5-7% CO_2. The cultures were scored periodically for 7 days for the presence or absence of unspecified cytopathic effects, cytotoxicity, and viability. Controls included those for input virus count, dried virus count, cytotoxicity, and neutralization (both product lots). Viral and cytotoxicity titers were calculated by the method of Spearman Karber.

Note: Protocol deviations/amendments reported in the study were reviewed.

4. MRID 486034-05 "Virucidal Efficacy of a Disinfectant for Use on Inanimate Environmental Surfaces, Virus: Rotavirus" for Edelweiss Trigger, by Mary J. Miller. Study conducted at ATS Labs. Study completion date – September 1, 2011. Amended report date – September 6, 2011. Study Identification Number A11717.

This study was conducted against Rotavirus (Strain WA; obtained from the University of Ottawa, Ontario, Canada), using MA-104 cells (Rhesus monkey kidney cells; obtained from Diagnostic Hybrids, Athens, OH; propagated in-house) as the host system. Two lots (Lot Nos. 1754-080 and 1754-081) of the product, Edelweiss Trigger Formula 1563-125A, were tested according to ATS Labs Protocol No. SRC53070811.ROT (copy provided). The product was received ready-to-use, as a trigger spray. The stock virus culture was adjusted to contain 1% fetal bovine serum as the organic soil load. Films of virus were prepared by spreading 0.2 mL of virus inoculum uniformly over the bottoms of separate sterile glass Petri dishes. The virus films were air-dried for 20 minutes at 20.0°C at 50% relative humidity. For each lot of product, separate dried virus films were sprayed (3 pumps) with the product from a distance of 6-8 inches from the carrier surface until thoroughly wet. The carriers were allowed to remain wet for 10 minutes at 20.0°C. Just prior to the end of the exposure time (≤15 seconds), the plates were scraped with a cell scraper to re-suspend the contents. The virus-disinfectant mixtures were passed immediately through individual Sephadex columns, and diluted serially in serum-free Minimum Essential Medium with 10 µg/mL gentamicin, 100 units/mL penicillin, 2.5 µg/mL amphotericin B, 0.5 µg/mL trypsin, and 2.0 mM L-glutamine. MA-104 cells in multi-well culture dishes were inoculated in quadruplicate with 0.1 mL of the dilutions. The inoculum was allowed to adsorb for 60 minutes at 36-38°C in a humidified atmosphere of 5-7% CO_2. Following adsorption, the cultures were re-fed and incubated at 36-38°C in a humidified atmosphere of 5-7% CO_2. The cultures were scored periodically for 7 days for the presence or absence of unspecified cytopathic effects, cytotoxicity, and viability. Controls included those for input virus count, dried virus count, cytotoxicity, and

neutralization (both product lots). Viral and cytotoxicity titers were calculated by the method of Spearman Karber.

Note: The initial laboratory report was amended to clarify the name of the tested product.

V RESULTS

MRID Number	Organism	No. Exhibiting Growth/ Total No. Tested			Carrier Population (average $\log_{10}$)
		Lot No. 1754-080	Lot No. 1754-081	Lot No. 1754-082	
10-Minute Exposure Time					
486034-02	*Staphylococcus aureus*				
	Test Date: 7/18/2011	0/60	0/60	---	6.22
	Test Date: 8/31/2011	---	---	0/60	6.38
486034-02	*Salmonella enterica*				
	Test Date: 7/18/2011	0/60	0/60	---	5.77
	Test Date: 8/31/2011	---	---	0/60	6.19
486034-03	*Pseudomonas aeruginosa*				
	Test Date: 7/18/2011	0/60	0/60	---	6.20
	Test Date: 8/31/2011	---	---	0/60	6.18

MRID Number	Organism	Results			Dried Virus Count
			Lot No. 1754-080	Lot No. 1754-081	
10-Minute Exposure Time					
486034-04	Rhinovirus type 37	10^{-1} dilution	Cytotoxicity	Cytotoxicity	$10^{4.50}$ $TCID_{50}$/0.1 mL
		10^{-2} to 10^{-8} dilutions	Complete inactivation	Complete inactivation	
		$TCID_{50}$/0.1 mL	$\leq 10^{1.50}$	$\leq 10^{1.50}$	
		Log reduction	≥ 3.00 $\log_{10}$	≥ 3.00 $\log_{10}$	
486034-05	Rotavirus	10^{-1} to 10^{-2} dilutions	Cytotoxicity	Cytotoxicity	$10^{7.50}$ $TCID_{50}$/0.1 mL
		10^{-3} to 10^{-8} dilutions	Complete inactivation	Complete inactivation	
		$TCID_{50}$/0.1 mL	$\leq 10^{2.50}$	$\leq 10^{2.50}$	
		Log reduction	≥ 5.00 $\log_{10}$	≥ 5.00 $\log_{10}$	

VI CONCLUSIONS

1. The submitted efficacy data support the use of the product, Edelweiss Trigger Formula 1563-125A, as a disinfectant with bactericidal activity against the following microorganisms on pre-cleaned, hard, non-porous surfaces for a 10-minute contact time:

Staphylococcus aureus	MRID 486034-02
Salmonella enterica	MRID 486034-02
Pseudomonas aeruginosa	MRID 486034-03

Complete killing was observed in the subcultures of the required number of carriers tested against the required number of product lots. At least one of the product lots tested was at least 60 days old at the time of testing. Neutralization confirmation testing showed positive growth of the microorganisms. Viability controls were positive for growth. Purity controls were reported as pure. Sterility controls did not show growth.

2. The submitted efficacy data support the use of the product, Edelweiss Trigger Formula 1563-125A, as a disinfectant with virucidal activity against the following microorganisms on hard, non-porous surfaces in the presence of a 1% organic soil load for a 10-minute contact time:

Rhinovirus type 37	MRID 486034-04
Rotavirus	MRID 486034-05

Recoverable virus titers of at least 10^4 were achieved. In studies against Rhinovirus type 37, cytotoxicity was observed in the 10^{-1} dilutions. In studies against Rotavirus, cytotoxicity was observed in the 10^{-1} and 10^{-2} dilutions. Complete inactivation (no growth) was indicated in all higher dilutions tested. At least a 3-log reduction in titer was demonstrated beyond the cytotoxic level.

VII RECOMMENDATIONS

1. The proposed label claims that the product, Edelweiss - Trigger, is an effective disinfectant against the following microorganisms on pre-cleaned, hard, non-porous surfaces for a 10-minute contact time.

Pseudomonas aeruginosa
Salmonella enterica
Staphylococcus aureus
Rhinovirus type 37
Rotavirus

These claims are acceptable as they are supported by the submitted data.

2. The following revisions to the proposed label are required/ recommended:

- On page 19 of the proposed label, change "Enamel" to read "Baked enamel." Enamel is a porous surface.
- On the proposed label, remove any statements regarding "active oxygen" and "oxygenated". This claim is unacceptable as it implies safety and environmental preference.
- On page 4 of the proposed label, the term "cold" must be qualified in the absence of data against Coronavirus and RSV.
- On pages 4, 5, and 6 of the proposed label, remove the statement "breaks down into water and oxygen". While this phrase may be chemically correct, it is unacceptable because it implies safety and environmental preference.
- On the proposed label, the term "powered" is only acceptable for non-pesticide claims.
- On page 6 of the proposed label, remove the claim "fast". The Agency has

not determined the contact time consistent of for fast. The Agency has determined that 10-seconds is consistent with the term "quick".

- On the proposed label, all allergen claims must the qualified as non-living.
- On page 10 of the proposed label, EET ha concerns about the quantitative implications of the claim "removes 90% of allergens".
- On page 12 of the proposed label, add the qualifier "from treated surfaces" to the claim "Reduces the amount of bacteria on a surface".

3. The proposed label states, on page 15, that the product is not recommended for use on finished wood surfaces. The proposed label states, on page 17, that the product is gentle on finished wood. The proposed label, on page 19, identifies finished wood floors as a surface on which the product may be used. These inconsistencies must be addressed.

4. The proposed label states, on page 15, that the product is not recommended for use on vinyl. The proposed label, on page 19, identifies vinyl as a surface on which the product may be used type. The proposed label, on page 19, identifies vinyl floors as a surface on which the product may be used. These inconsistencies must be addressed.